

## **REMARKS**

Claims 1, 9-10, 15-16 and 40 have been amended and are fully supported by the specification and original claims. The amendment to claim 1 is supported at page 2, lines 13-14 of the specification. Applicants thank the Examiner for his suggestions regarding punctuation of the claims, and the remaining amendments are made to adopt those suggestions.

In the July 1, 2008, Office Action, claims 1-4, 9-12, 4-17 and 40-41 were rejected under 35 USC § 112 ¶ 1 for lack of written description. Claims 15 and 40-41 were rejected under 35 USC § 112 ¶ 2 as indefinite. Additionally, claims 9-10, 16 and 40 are objected to for grammatical reasons. The specific grounds for rejection, and applicants' response thereto, are set forth in detail below.

### **Objections**

Applicants have amended claims 9-10, 16 and 40 by inserting commas as per the Examiners instructions and, accordingly, withdrawal of the objections respectfully is requested.

### **Rejections Under 35 USC § 112 ¶ 1**

Claims 1-4, 9-12, 4-17 and 40-41 stand rejected under 35 USC § 112 ¶ 1 as failing to comply with the written description requirement. Applicants respectfully traverse.

The Examiner states that the "structure of the claimed invention does not fit the ... written description because ... there is no description of chemically fixed biological sample." (Office Action at page 5). Applicants respectfully submit that the nature of chemically fixed biological samples is well known in the art, and is described in paragraph 3 of the published application. Nevertheless, without acquiescing in the propriety of the rejection, and purely to progress the application toward allowance, applicants have amended claim 1 to recite "formalin" instead of "chemical fixative." As the Examiner notes on page 5 of the Office Action, formalin fixed biological samples are recited in the specification at page 1, lines 25-34 and have written description support.

The Examiner also states that while organic solvents are defined in the specification, "there is no precise description of removing paraffin in said biological sample by "adding an organic solvent."" Applicants respectfully do not understand the rejection. Removing paraffin

from biological samples by using an organic solvent is a technique that is well known in the art. It is axiomatic that an application need not describe, and preferably omits, what is well known in the art. *Falkner v. Inglis*, 448 F.3d 1357, 1365 (Fed. Cir. 2006), quoting *Spectra-Physics, Inc. v. Coherent, Inc.* 827 F.2d 1524, 1534 (Fed. Cir. 1987). As evidence that the use of organic solvents for removing paraffin from biological samples is a technique that is well known in the art, applicants provide the attached Declaration of Dr. Anirban Maitra (the "Maitra Declaration"). Dr Maitra describes how samples are embedded in paraffin, and explains in detail the steps for subsequent removal of the paraffin. Dr. Maitra also describes the variety of solvents that can be used for removing paraffin and that the use organic solvent is a technique that is well known to one skilled in the art.

The Examiner also states that the physical and/or chemical properties of (a) a chemically fixed sample and (b) the organic solvents to remove paraffin from the biological samples is not of record in the specification (see Office Action page 5). With respect to point (a), applicants have amended claim 1 to recite that the sample is formalin fixed, and have deleted the term "chemically," thereby obviating the rejection. Nevertheless, the Maitra Declaration describes the steps of chemical fixation and states that these steps have been know in the art for many decades. See Maitra Declaration at paragraph 4. The Maitra Declaration also describes the entire process from fixation to embedding to deparaffinization and shows that this is a process that is well understood in the art. Briefly, a sample is placed in a fixative, such as formalin, and covalent bonds are formed between the fixative and the amine groups of the tissue proteins, causing cross-linking of the proteins. Once fixed, the samples are embedded in, for example, paraffin. Samples are then sectioned onto slides. Lastly, the paraffin is removed by dipping/washing the slides in an organic solvent and then processing the sample in alcohol. See Maitra Declaration at paragraphs 5-7.

The Examiner raises the same objections to questions about the organic solvents used to deparaffinize samples as previously raised with the chemically fixed samples, and applicants again direct the Examiner to the Maitra Declaration. At paragraph 6, the declaration states that "[t]he physical and chemical properties of organic solvents used to solubilize paraffin for deparaffinization of samples would have been well known to one having ordinary skill in the art." Moreover, elementary textbooks of organic chemistry and countless standard reference books describe the chemical and physical properties of xylene, benzene, chloroform, hexanes

and heptanes and the like. See, for example, the famous “Rubber Handbook” (*CRC Handbook of Chemistry and Physics*) which is now in its 85<sup>th</sup> edition, and which describes the properties of these solvents and countless others. One skilled in the art would readily be aware of the chemical and physical properties of the solvents that might be used for removing paraffin from tissue samples.

Accordingly, because the physical and chemical properties would have been known to one of ordinary skill in the art, the written description requirement is met and the rejection should be withdrawn.

### **Rejections Under 35 USC § 112 ¶ 2**

Claims 15 and 40-41 are rejected under 35 USC § 112 ¶ 2 as indefinite. Applicants respectfully traverse.

First, the Examiner states that claim 15 lacked antecedent basis for the term “multi-use.” The term “multi-use” has been deleted from claim 15, thereby mooted the rejection.

Second, the Examiner states that the phrase “drip column fractionation” renders claim 40 “incomprehensible, unclear and vague,” because the metes and bounds are not defined either in the claims or specification (see office action pages 6-7). Applicants respectfully submit that the term “drip column fractionation” is a term of art that refers to a technique used by chemists and biochemists to separate samples and would have been well known to the skilled artisan. Indeed, the Maitra Declaration provides a number of references that discuss this type of chemical separation technique (see Maitra Declaration at appendix B). Accordingly, because the term “drip column fractionation” has a meaning that is well understood by those skilled in the art, it clearly complies with the requirements of § 112, second paragraph, and applicants respectfully request withdrawal of the rejection.

Third, claim 41 recites the phrase, “further comprising assaying said lysate using mass spectrometry.” The Examiner rejects claim 41 for insufficient antecedent basis stating that claim 1, from which claim 41 depends through claim 15, is “not drawn only to a method to prepare ‘biomolecule lysate.’” (see office action at page 7). Applicants respectfully submit that it is perfectly clear that under conventional standards of grammar and claim construction the “lysate” referred to in claim 41 is the “biomolecule lysate” of claim 1 and that one skilled in the art would

understand as much. Nevertheless, without acquiescing in the propriety of the rejection, and purely to progress the application toward allowance, applicants have amended claim 41 to recite "said biomolecule lysate," thereby obviating the rejection.

**CONCLUSION**

In view of the foregoing amendments and remarks, applicants respectfully submit that the application is in condition for allowance. Should the Examiner feel that there are any issues outstanding after consideration of this response, the Examiner is invited to contact the undersigned to expedite prosecution of the application.

The Commissioner is hereby authorized by this paper to charge any fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-3840. **This paragraph is intended to be a CONSTRUCTIVE PETITION FOR EXTENSION OF TIME in accordance with 37 C.F.R. § 1.136(a)(3).**

Respectfully submitted,



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